IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Desjarlais, J.
Serial No.:	10/071,859
Filed:	February 6, 2002
For:	APPARATUS AND METHOD FOR DESIGNING PROTEINS AND PROTEIN LIBRARIES
Examiner:	Not Yet Assigned
Group Art Unit:	Not Yet Assigned
Attorney Docket No.:	823.0093USQ

Assistant Commissioner for Patents
Washington, DC 20231

PRELIMINARY AMENDMENT

Dear Sir:

Prior to substantive examination, please make the following amendments to the claims.

In the Claims

Please cancel claims 1-15 without prejudice or disclaimer.

Please add the following new claims:

--18. (New) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

a) inputting a protein backbone scaffold;

b) applying a first protein design cycle comprising at least one heuristic component to said scaffold to generate at least a first variable sequence;

c) applying a second protein design cycle comprising at least one heuristic component to said scaffold to generate at least a second variable sequence; and

d) generating a probability matrix comprising at least said first and second variable sequences.

19. (New) A method according to claim 18 wherein said first and second protein design cycle comprise the same components.

20. (New) A method according to claim 18 wherein said first and second protein design cycle comprise different components.

21. (New) A method according to claim 18 wherein at least one of said heuristic components comprises a genetic algorithm.

22. (New) A method according to claim 18 wherein at least one of said heuristic components comprises a Monte Carlo algorithm.

23. (New) A method according to claim 21 wherein at least one of said first and second protein design cycles comprises a self consistent mean field theory (SCMF) algorithm.

24. (New) A method according to claim 22 wherein at least one

of said first and second protein design cycles comprises a self consistent mean field theory (SCMF) algorithm.

25. (New) A method according to claim 21 wherein at least one of said first and second protein design cycles comprises a dead end elimination (DEE) algorithm.

26. (New) A method according to claim 22 wherein at least one of said first and second protein design cycles comprises a dead end elimination (DEE) algorithm.

27. (New) A method according to claim 18 wherein said probability matrix comprises a summation of the variable sequences generated for each scaffold.

28. (New) A method according to claim 18 wherein said probability matrix comprises a recombination of some or all of the variable sequences generated for each scaffold.

29. (New) A method according to claim 18 further comprising ranking said variable sequences.

30. (New) A method according to claim 18 further comprising synthesizing a plurality of said sequences

31. (New) A method according to claim 18 further comprising recombining a plurality of said variable sequences to form additional variable sequences.

32. (New) A method executed by a computer under the control of a

program, said computer including a memory for storing said program, said method comprising the steps of:

a) inputting an ensemble of protein backbone scaffolds;

b) applying a protein design cycle to each of said scaffolds to generate at least one variable sequence; and

c) generating a probability matrix comprising a plurality of the variable sequences generated in step b).

33. (New) A method according to claim 32 wherein said probability matrix comprises a summation of the variable sequences generated for each scaffold.

34. (New) A method according to claim 32 wherein said probability matrix comprises a recombination of some or all of the variable sequences generated for each scaffold.

35. (New) A method according to claim 32 wherein said protein design cycle comprises a genetic algorithm.

36. (New) A method according to claim 32 wherein said protein design cycle comprises a Monte Carlo algorithm.

37. (New) A method according to claim 32 wherein said protein design cycle comprises a self consistent mean field theory (SCMF) algorithm.

38. (New) A method according to claim 32 wherein said protein design cycle comprises a dead end elimination (DEE) algorithm.

39. (New) A method according to claim 32 wherein said ensemble comprises a family of naturally occurring proteins.

40. (New) A method according to claim 32 wherein said ensemble is generated by a Monte Carlo simulation.

41. (New) A method according to claim 32 further comprising ranking said variable sequences.

42. (New) A method according to claim 32 further comprising synthesizing a plurality of said sequences.

43. (New) A method according to claim 32 further comprising recombining a plurality of said variable sequences to form additional variable sequences.

44. (New) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

a) inputting at least one protein backbone scaffold;

b) applying a protein design cycle to generate at least a first variable nucleated state sequence;

c) sequentially altering in said nucleated state sequence a plurality of amino acids by testing a plurality of rotamers for each amino acid change and calculating the energy of each altered sequence; and

d) generating a Boltzmann probability matrix comprising a plurality of altered nucleated state sequences.

45. (New) A method according to claim 44 wherein an ensemble of protein backbone scaffolds are inputted.

46. (New) A method according to claim 44 further comprising ranking said altered nucleated state sequences.

47. (New) A method according to claim 44 further comprising synthesizing a plurality of said altered nucleated state sequences.--

REMARKS

Claims 1-15 have been cancelled without prejudice or disclaimer. Claims 18-47 are newly added. Claims 16-47 are now pending. An appendix of "PENDING CLAIMS" is attached for the Examiner's convenience.

Support for new claims 18-25 can be found in various places in the specification, for example at page 5, lines 18-22 and Figure 2.

Support for new claims 27-38 can be found throughout the specification, for example at page 3, lines 6-14; page 19, lines 25-33. Additional support can be found in original claims 1-14.

Support for new claims 29 and 46 can be found at page 3, lines 20-21 and page 5, lines 18-22.

Support for new claim 30 and 47 can be found at page 3, lines 20-21 and page 30, lines 21-32.

Support for new claims 44-45 can be found in various places in the specification, for example at page 20, lines 16-27; page 23, lines 8-43.

Consideration and allowance, being in order, are earnestly solicited. If the Examiner has further questions regarding the application, the undersigned would welcome a telephone call at (203) 327-4500.

April 10, 2002
Date

Respectfully submitted,

Paul D. Greeley, Esq.
Reg. No. 31,019
Ohlandt, Greeley, Ruggiero & Perle, L.L.P.
One Landmark Square, 10th Floor
06901-2682

PENDING CLAIMS

16. A method for optimizing simulation or scoring function parameters that utilizes comparisons between designed sequences and natural sequences, comprising the steps of:

a) applying a protein design cycle to produce a variable protein sequence;

b) comparing said variable protein sequence to at least one natural protein sequence and/or conformation;

c) modifying said simulation or scoring function parameters to reflect said comparison.

17. A method for optimizing simulation or scoring function parameters that utilizes comparisons between designed sequences and natural sequences, comprising the steps of:

a) applying a protein design cycle to produce an amino acid probability matrix;

b) comparing said matrix to at least one natural protein sequence and/or conformation;

c) modifying said simulation or scoring function parameters to reflect said comparison.

--18. (New) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

d) inputting a protein backbone scaffold;

e) applying a first protein design cycle comprising at least one heuristic component to said scaffold to generate at least a first variable sequence;

f) applying a second protein design cycle comprising at least one heuristic component to said scaffold to generate at least a second variable sequence; and

d) generating a probability matrix comprising at least said first and second variable sequences.

19. (New) A method according to claim 18 wherein said first and second protein design cycle comprise the same components.

20. (New) A method according to claim 18 wherein said first and second protein design cycle comprise different components.

21. (New) A method according to claim 18 wherein at least one of said heuristic components comprises a genetic algorithm.

22. (New) A method according to claim 18 wherein at least one of said heuristic components comprises a Monte Carlo algorithm.

27. (New) A method according to claim 21 wherein at least one of said first and second protein design cycles comprises a self consistent mean field theory (SCMF) algorithm.

28. (New) A method according to claim 22 wherein at least one

of said first and second protein design cycles comprises a self consistent mean field theory (SCMF) algorithm.

29. (New) A method according to claim 21 wherein at least one of said first and second protein design cycles comprises a dead end elimination (DEE) algorithm.

30. (New) A method according to claim 22 wherein at least one of said first and second protein design cycles comprises a dead end elimination (DEE) algorithm.

27. (New) A method according to claim 18 wherein said probability matrix comprises a summation of the variable sequences generated for each scaffold.

28. (New) A method according to claim 18 wherein said probability matrix comprises a recombination of some or all of the variable sequences generated for each scaffold.

29. (New) A method according to claim 18 further comprising ranking said variable sequences.

30. (New) A method according to claim 18 further comprising synthesizing a plurality of said sequences

31. (New) A method according to claim 18 further comprising recombining a plurality of said variable sequences to form additional variable sequences.

33. (New) A method executed by a computer under the control of a

program, said computer including a memory for storing said program, said method comprising the steps of:

c) inputting an ensemble of protein backbone scaffolds;

d) applying a protein design cycle to each of said scaffolds to generate at least one variable sequence; and

c) generating a probability matrix comprising a plurality of the variable sequences generated in step b).

33. (New) A method according to claim 32 wherein said probability matrix comprises a summation of the variable sequences generated for each scaffold.

34. (New) A method according to claim 32 wherein said probability matrix comprises a recombination of some or all of the variable sequences generated for each scaffold.

35. (New) A method according to claim 32 wherein said protein design cycle comprises a genetic algorithm.

36. (New) A method according to claim 32 wherein said protein design cycle comprises a Monte Carlo algorithm.

37. (New) A method according to claim 32 wherein said protein design cycle comprises a self consistent mean field theory (SCMF) algorithm.

38. (New) A method according to claim 32 wherein said protein design cycle comprises a dead end elimination (DEE) algorithm.

39. (New) A method according to claim 32 wherein said ensemble comprises a family of naturally occurring proteins.

40. (New) A method according to claim 32 wherein said ensemble is generated by a Monte Carlo simulation.

41. (New) A method according to claim 32 further comprising ranking said variable sequences.

42. (New) A method according to claim 32 further comprising synthesizing a plurality of said sequences.

43. (New) A method according to claim 32 further comprising recombining a plurality of said variable sequences to form additional variable sequences.

45. (New) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

e) inputting at least one protein backbone scaffold;

f) applying a protein design cycle to generate at least a first variable nucleated state sequence;

g) sequentially altering in said nucleated state sequence a plurality of amino acids by testing a plurality of rotamers for each amino acid change and calculating the energy of each altered sequence; and

h) generating a Boltzmann probability matrix comprising a plurality of altered nucleated state sequences.

45. (New) A method according to claim 44 wherein an ensemble of protein backbone scaffolds are inputted.

46. (New) A method according to claim 44 further comprising ranking said altered nucleated state sequences.

47. (New) A method according to claim 44 further comprising synthesizing a plurality of said altered nucleated state sequences.--